

Listing of the Claims

This listing of the claims replaces all prior versions and listings:

1. (currently amended): A method for establishing an association between a first gene and a selected phenotype in a cell, the method comprising the steps of:
 - (i) selecting a first gene, wherein the first gene is not operably linked to heterologous sequences,
 - (ii) selecting a second gene, wherein the second gene is different from the first gene and wherein the second gene is not operably linked to heterologous sequences;
 - (iii) providing a first polynucleotide comprising a sequence encoding a first zinc finger protein operably linked to a promoter, wherein the first zinc finger protein binds to a first target site in the first gene and modulates expression of the first gene;
 - (iv) providing a second polynucleotide comprising a sequence encoding a second zinc finger protein operably linked to a promoter, wherein the second zinc finger protein binds to a second target site in the second gene and modulates expression of the second gene;
 - (v) administering the first polynucleotide to a first cell and culturing the first cell under conditions where the first zinc finger protein is expressed and contacts the first gene;
 - (vi) administering the second polynucleotide to a second cell and culturing the second cell under conditions where the second zinc finger protein is expressed and contacts the second gene; and
 - (vii) assaying the first and second cells for the selected phenotype, wherein a change in the selected phenotype in the first cell as compared to the second cell indicates an association between the first gene and the selected phenotype.
2. (previously presented) The method of claim 1, further comprising providing a third polynucleotide comprising a sequence encoding a third zinc finger protein operably linked to a promoter, wherein the third zinc finger protein binds to a third target site in the first gene, wherein the third target site is different than the first target site.

3 to 4. (canceled).

5. (previously presented): The method of claim 1, wherein the first gene comprises an EST.
6. (previously presented): The method of claim 1, wherein the first and second cells are derived from the same cell type.
7. (canceled).
8. (previously presented): The method of claim 1, wherein the first and the second genes are endogenous cellular genes.
9. (previously presented): The method of claim 1, wherein the modulation is repression.
10. (previously presented): The method of claim 1, wherein the modulation is activation.
11. (currently amended): The method of claim 1, wherein each zinc finger protein is a fusion proteins protein further comprising a regulatory domain.
12. (previously presented): The method of claim 11, wherein the function of the regulatory domain is under small molecule control.
13. (previously presented): The method of claim 11, wherein at least one zinc finger protein is a fusion protein comprising at least two regulatory domains.
14. (currently amended): The method of claim 1, wherein the cell is selected from the group consisting of an animal cell, a plant cell, a bacterial cell, a protozoal cell, or and a fungal cell.
15. (original): The method of claim 14, wherein the cell is a mammalian cell.
16. (currently amended): The method of claim 15, wherein the cell is a human cell.

17. (original): The method of claim 1, wherein expression is activation of gene expression that prevents repression of gene expression.

18. (original): The method of claim 1, wherein the modulation of expression is inhibition of gene expression that prevents gene activation.

19. (original): The method of claim 11, wherein the regulatory domain is selected from the group consisting of a transcriptional repressor, a methyl transferase, a transcriptional activator, a histone acetyltransferase, and histone deacetylase.

20 to 23. (canceled).

24. (previously presented): The method of claim 1, wherein the first or second polynucleotide is contained in a viral expression vector.

25. (original): The method of claim 24, wherein the expression vector is a retroviral expression vector, an adenoviral expression vector, or an AAV expression vector.

26. (previously presented): The method of claim 1, wherein at least one of the promoters is an inducible promoter.

27. (original): The method of claim 1, wherein the cell comprises less than about 1.5×10^6 copies of the zinc finger protein.

28. (previously presented): The method of claim 1, wherein expression of one or more of the zinc finger proteins encoded by the first or second polynucleotides is induced by administration of an exogenous agent.

29. (previously presented): The method of claim 1, wherein the sequences encoding the first and second zinc finger proteins are operably linked to different promoters.

30. (previously presented): The method of claim 1, wherein expression of the first zinc finger protein is controlled by a small molecule.

31. (previously presented): The method of claim 1, wherein expression of the second zinc finger protein is controlled by a small molecule.

32. (previously presented): The method of claim 1, wherein expression of both the first and second zinc finger proteins encoded by the first and second polynucleotides are controlled by a small molecule.

33. (previously presented): The method of claim 32, wherein expression of the first zinc finger protein and expression of the second zinc finger protein are controlled by different small molecules.

34 to 86. (canceled).

87. (previously presented): A method for determining the association between a gene and a phenotype of a cell, the method comprising the steps of:

(i) providing first, second and third cells,
(ii) contacting the first cell with a first polynucleotide comprising a sequence encoding a first zinc finger protein operably linked to a promoter, wherein the first zinc finger protein binds to a first target site in the gene and activates expression of the gene;

(iii) contacting the second cell with a second polynucleotide comprising a sequence encoding a second zinc finger protein operably linked to a promoter, wherein the second zinc finger protein binds to a second target site in the gene and represses expression of the gene;

(iv) assaying the first, second and third cells for the selected phenotype; and
(v) comparing the phenotypes exhibited by the first, second and third cells, wherein if the first or second cell exhibits a different phenotype than the third cell, the gene is associated with the phenotype.

88. (previously presented): The method of claim 87, wherein first and second target sites are different.

89. (previously presented): The method of claim 87, wherein first and second target sites are the same.

90. (previously presented): The method of claim 87, wherein at least one of the first and second zinc finger proteins further comprises a regulatory domain.

91. (previously presented): The method of claim 90, wherein both first and second zinc finger proteins both further comprise a regulatory domain and further wherein the regulatory domains are the same.

92. (previously presented): The method of claim 90, wherein function of the regulatory domain is dependent on a small molecule.

93. (previously presented): The method of claim 87, further comprising the step of exposing the first, second and third cells to at least one selected stimulus prior to assaying for a selected phenotype.

94. (previously presented): The method of claim 93, wherein the phenotype assayed is a change in cell physiology.

95. (previously presented): The method of claim 93, wherein the selected stimulus is serum starvation, growth factor depletion or growth factor stimulation.

96. (previously presented): The method of claim 95, wherein the phenotype assayed is cell proliferation.

97. (previously presented): The method of claim 96, wherein the phenotype assayed is a change in cell cycling.

98. (previously presented): The method of claim 93, wherein the selected stimulus is stress.

99. (previously presented): The method of claim 98, wherein the stress is selected from the group consisting of reducing agents, oxidizing agents, mutagens, DNA

synthesis inhibitors, DNA damaging agents, heat shock, cold shock, hypoxia, and altered pressure.

100. (previously presented): The method of claim 99, wherein the DNA damaging agent is a chemical.

101. (previously presented): The method of claim 99, wherein the DNA damaging agent is irradiation.

102. (previously presented): The method of claim 98, wherein the phenotype assayed is a change in cell metabolism.

103. (previously presented): The method of claim 102, wherein the change in cell metabolism is assayed using a transformation assay.

104. (previously presented): The method of claim 93, wherein the selected stimulus is exposure to a pathogen.

105. (previously presented): The method of claim 104, wherein the pathogen is a bacterium.

106. (previously presented): The method of claim 104, wherein the pathogen is a virus.

107. (previously presented): The method of claim 104, wherein the pathogen is a unicellular eukaryote.

108. (previously presented): The method of claim 93, wherein the selected stimulus is treatment with a compound.

109. (previously presented): The method of claim 87, wherein the first, second and third cells further comprise an exogenous nucleic acid.

110. (previously presented): The method of claim 109, wherein the exogenous nucleic acid encodes a polypeptide.

111. (previously presented): The method of claim 110, wherein the polypeptide is an endogenous polypeptide.

112. (previously presented): The method of claim 110, wherein the polypeptide is a mutant form of an endogenous polypeptide.

113. (previously presented): The method of claim 87, wherein the association between the gene and the phenotype indicates a biological function of the gene.